



[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Prospective Grant of Exclusive Patent License: The Development of an Anti-mesothelin Recombinant Immunotoxin (RIT) for the Treatment of Human Cancers.

AGENCY: National Institutes of Health

ACTION: Notice

SUMMARY: The National Cancer Institute, National Institutes of Health, Department of Health and Human Services, is contemplating the grant of an Exclusive Patent License to Selecta Biosciences (“Selecta”) located in Watertown, Massachusetts to practice the inventions embodied in the patent applications listed in the Supplementary Information section of this notice.

DATES: Only written comments and/or applications for a license which are received by the NCI Technology Transfer Center on or before [INSERT DATE 15 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER] will be considered.

ADDRESSES: Requests for copies of the patent applications, inquiries, and comments relating to the contemplated Exclusive Patent License should be directed to: David A.

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SUPPLEMENTARY INFORMATION:

The following represents the intellectual property to be licensed under the prospective agreement:

US Patent Application 61/535,668 (HHS Ref. E-263-2011/0-US-01), PCT Application PCT/US2012/055034 (HHS reference E-263-2011/0-PCT-02), Australian Patent Application 2012308591 (HHS reference E-263-2011/0-AU-03), Canadian Patent Application 2846608 (HHS reference E-263-2011/0-CA-04), European Patent Application 12766780.6 (HHS reference E-263-2011/0-EP-05), US Patent 9,206,240 (HHS reference E-263-2011/0-US-06), Hong Kong Patent Application 14111650.2 (HHS reference E-263-2011/0-HK-07), and US Patent Application 14/927,645 (HHS reference E-263-2011/0-US-08);

US Patent Application 61/495,085 (HHS Ref. E-174-2011/0-US-01), PCT Application PCT/US2012/041234 (HHS reference E-174-2011/0-PCT-02), Australian Patent Application 2012268013 (HHS reference E-174-2011/0-AU-03), Brazilian Patent Application 112013031262-9 (HHS reference E-174-2011/0-BR-04), Canadian Patent Application 2838013 (HHS reference E-174-2011/0-CA-05), Chinese Patent Application 201280039071.1 (HHS reference E-174-2011/0-CN-06), European Patent Application 12727074.2 (HHS reference E-174-2011/0-EP-07), Hong Kong Patent Application 14105911.9 (HHS reference E-174-2011/0-HK-08), Japanese Patent Application 2014-514616 (HHS reference E-174-2011/0-JP-09), South Korean Patent Application 2013-7032402 (HHS reference E-174-2011/0-KR-10), Mexican Patent Application

MX/a/2013/014388 (HHS reference E-174-2011/0-MX-11), Russian Patent Application 2013151655 (HHS reference E-174-2011/0-RU-12), US Patent 9,346,859 (HHS reference E-174-2011/0-US-13), Hong Kong Patent Application 14106689.7 (HHS reference E-174-2011/0-HK-14), and US Patent Application 15/095,470 (HHS reference E-174-2011/0-US-15);

US Patent Application 61/483,531 (HHS Ref. E-117-2011/0-US-01), PCT Application PCT/US2012/036456 (HHS reference E-117-2011/0-PCT-02), Australian Patent Application 2012253896 (HHS reference E-117-2011/0-AU-03), Brazilian Patent Application 112013028537-0 (HHS reference E-117-2011/0-BR-04), Canadian Patent Application 2835070 (HHS reference E-117-2011/0-CA-05), Chilean Patent Application 03182-2013 (HHS reference E-117-2011/0-CL-06), Ecuadorian Patent Application SP-13-13067 (HHS reference E-117-2011/0-EC-07), Egyptian Patent Application PCT 1697/2013 (HHS reference E-117-2011/0-EG-08), European Patent Application 12722586.0 (HHS reference E-117-2011/0-EP-09), Hong Kong Patent Application 14105586.3 (HHS reference E-117-2011/0-HK-10), South Korean Patent Application 2013-7032247 (HHS reference E-117-2011/0-KR-11), Mexican Patent Application MX/a/2013/012905 (HHS reference E-117-2011/0-MX-12), Malaysian Patent Application PI2013702094 (HHS reference E-117-2011/0-MY-13), New Zealand Patent Application 617386 (HHS reference E-117-2011/0-NZ-14), Philippines Patent Application 1-2013-502264 (HHS reference E-117-2011/0-PH-15), Russian Patent Application 2013148919 (HHS reference E-117-2011/0-RU-16), Singapore Patent Application 201308179-9 (HHS reference E-117-2011/0-SG-17), Thailand Patent

Application 1301006329 (HHS reference E-117-2011/0-TH-18), Ukrainian Patent
 Application 201313011 (HHS reference E-117-2011/0-UA-19), Vietnamese Patent
 Application 1-2013-03855 (HHS reference E-117-2011/0-VN-20), South African Patent
 Application 2013/08270 (HHS reference E-117-2011/0-ZA-21), US Patent Application
 14/115,131 (HHS reference E-117-2011/0-US-22), Japanese Patent Application 2014-
 509467 (HHS reference E-117-2011/0-JP-23), Chinese Patent 201280033583.7 (HHS
 reference E-117-2011/0-CN-24), Colombian Patent Application 13-274.153 (HHS
 reference E-117-2011/0-CO-25), Costa Rican Patent Application 2013-0571 (HHS
 reference E-117-2011/0-CR-26), Indonesian Patent Application W-00201305198 (HHS
 reference E-117-2011/0-ID-27), Israeli Patent Application 229198 (HHS reference E-
 117-2011/0-IL-28), Indian Patent Application 8854/CHENP/2013 (HHS reference E-117-
 2011/0-IN-29), Peruvian Patent Application 2456.13 (HHS reference E-117-2011/0-PE-
 30), Algerian Patent Application 130758 (HHS reference E-117-2011/0-DZ-31),
 Moroccan Patent Application 36534 (HHS reference E-117-2011/0-MA-32), and Hong
 Kong Patent Application 14108273.5 (HHS reference E-117-2011/0-HK-33);

U.S. Patent Application 61/241,620 (HHS Ref. E-269-2009/0-US-01), PCT Application
 PCT/US2010/048504 (HHS reference E-269-2009/0-PCT-02), Australian Patent
 2010292069 (HHS reference E-269-2009/0-AU-03), Canadian Patent Application
 2773665 (HHS reference E-269-2009/0-CA-04), Chinese Patent 201080049559.3 (HHS
 reference E-269-2009/0-CN-05), European Patent 2475398 (HHS reference E-269-
 2009/0-EP-06), as validated in France, Germany, Italy, Spain and the United Kingdom,
 Indian Patent Application 3197/CHENP/2012 (HHS reference E-269-2009/0-IN-07),

Japanese Patent 5795765 (HHS reference E-269-2009/0-JP-08), Russian Patent Application 2012114005 (HHS reference E-269-2009/0-RU-09), and US Patent 8,936,792 (HHS reference E-269-2009/0-US-10);

U.S. Patent Application 60/969,929 (HHS Ref. E-292-2007/0-US-01), PCT Application PCT/US2008/075296 (HHS reference E-292-2007/0-PCT-02), Australian Patent 2008296194 (HHS reference E-292-2007/0-AU-03), Canadian Patent Application 2698357 (HHS reference E-292-2007/0-CA-04), European Patent 2197903 (HHS reference E-292-2007/0-EP-05) as validated in Austria, Belgium, Bulgaria,, Switzerland, Cyprus, Germany, Denmark, Estonia, Spain, Finland, France, the United Kingdom, Greece, Croatia, Hungary, Ireland, Italy, Lithuania, Luxembourg, Latvia, Monaco, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Slovakia, and Turkey, US Patent 8,871,906 (HHS reference E-292-2007/0-US-06), European Patent Application 12184319.7 (HHS reference E-292-2007/0-EP-07), and Hong Kong Patent Application 13106628.2 (HHS reference E-292-2007/0-HK-08);

U.S. Patent Application 60/703,798 (HHS Ref. E-262-2005/0-US-01), PCT Application PCT/US2006/028986 (HHS reference E-262-2005/0-PCT-02), Australian Patent 2006275865 (HHS reference E-262-2005/0-AU-03), Canadian Patent 2616987 (HHS reference E-262-2005/0-CA-04), European Patent 1910407 (HHS reference E-262-2005/0-EP-05) as validated in Switzerland, Germany, Spain, France, the United Kingdom, and Italy, US Patent 8,907,060 (HHS reference E-262-2005/0-US-06), European Patent 2311854 (HHS reference E-262-2005/0-EP-07) as validated in

Switzerland, Germany, Spain, France, the United Kingdom, and Italy, European Patent 2332970 (HHS reference E-262-2005/0-EP-08) as validated in Germany, Spain, France, the United Kingdom, and Italy, Australian Patent 2012216642 (HHS reference E-262-2005/0-AU-15), Australian Patent 2014208269 (HHS reference E-262-2005/0-AU-22), European Patent Application 15191388.6 (HHS reference E-262-2005/0-EP-28), European Patent Application 15191391.0 (HHS reference E-262-2005/0-EP-29), European Patent Application 15191395.1 (HHS reference E-262-2005/0-EP-30), Australian Patent Application (HHS reference E-262-2005/0-AU-31), and Canadian Patent Application (HHS reference E-262-2005/0-CA-32);

U.S. Patent Application 60/160,071 (HHS Ref. E-139-1999/0-US-01), PCT Application PCT/US00/14829 (HHS reference E-139-1999/0-PCT-02), Canadian Patent 2374398 (HHS reference E-139-1999/0-CA-03), European Patent 1180123 (HHS reference E-139-1999/0-EP-04) as validated in Belgium, Switzerland, Germany, Denmark, France, The United Kingdom, Italy, The Netherlands, and Sweden, Japanese Patent 5683766 (HHS reference E-139-1999/0-JP-05), Mexican Patent 270476 (HHS reference E-139-1999/0-MX-06); and U.S. Patent 7,081,518 (HHS reference E-139-1999/0-US-07);

U.S. Patent Application 60/067,175 (HHS Ref. E-021-1998/0-US-01), PCT Application PCT/US98/25270 (HHS reference E-021-1998/0-PCT-02), Australian Patent 760120 (HHS reference E-021-1998/0-AU-03), Canadian Patent 2318576 (HHS reference E-021-1998/0-CA-04), European Patent 1025230 (HHS reference E-021-1998/0-EP-05) as validated in Switzerland, Germany, France, Italy, Spain and the United Kingdom, Israeli

Patent 135775 (HHS reference E-021-1998/0-IL-06), US Patent 6,809,184 (HHS reference E-021-1998/0-US-07), US Patent 7,368,110 (HHS reference E-021-1998/0-US-08), and US Patent 7,709,252 (HHS reference E-021-1998/0-US-15),

U.S. Patent Application 60/010,166 (HHS Ref. E-002-1996/0-US-01), PCT Application PCT/US97/00224 (HHS Ref. E-002-1996/1-PCT-01), U.S. Patent 6,083,502 (HHS reference E-002-1996/1-US-02), Australian Patent 703769 (HHS reference E-002-1996/1-AU-03), Canadian Patent 2241604 (HHS reference E-002-1996/1-CA-04), European Patent 0871492 (HHS reference E-002-1996/1-EP-05) as validated in Switzerland, Germany, France, Italy Spain and the United Kingdom, U.S. Patent 6,153,430 (HHS reference E-002-1996/1-US-14), and U.S. Patent 7,375,183 (HHS reference E-002-1996/1-US-15);

and all continuing applications and foreign counterparts.

With respect to persons who have an obligation to assign their right, title and interest to the Government of the United States of America, the patent rights in these inventions have been assigned to the Government of the United States of America.

The prospective Exclusive Patent License territory may be worldwide for the following field of use:

“The use of anti-mesothelin targeted immunotoxins for the treatment of mesothelin-expressing cancers, wherein the immunotoxins have:

- 1) A targeting domain containing the complementary determining regions (CDRs) of the SS1 antibody; and
- 2) A *Pseudomonas* exotoxin A (PE) toxin domain that lacks at least one B cell or T cell epitope due to the alteration or deletion of one or more amino acids.

For purposes of clarity, the immunotoxin may include additional alterations to B cell and T cell epitopes for the reduction of immunogenicity, a peptide linker sequence, and/or polyethylene glycol molecule(s). The immunotoxins may also be combined with the use of synthetic vaccine particle (SVP)-rapamycin.”

The present inventions to be licensed concern RITs which are targeted to mesothelin-expressing cancer cells, and methods of using the immunotoxins for the treatment of mesothelin-expressing cancers (such as mesothelioma, ovarian cancer and pancreatic cancer). The specific immunotoxin will have an antibody targeting domain that contains the CDRs of the antibody identified as SS1, which was invented at the NIH. The specific immunotoxin will also have a toxin domain derived from PE that is resistant to lysosomal proteases due to the deletion of a large portion of the exotoxin, and which lacks at least one major B-cell epitope due to the alteration an amino acid. Ultimately, the PE used in the immunotoxin may lack multiple B-cell epitopes, as well as multiple T-cell epitopes, in an effort to minimize immunogenicity.

Alterations to the toxin that reduce immunogenicity improve the therapeutic value of the immunotoxin while maintaining its ability to trigger cell death. Since mesothelin is

preferentially expressed on certain types of cancer cells, the immunotoxins selectively bind and kill only those cancer cells, allowing healthy, essential cells to remain unharmed. This may result in an effective therapeutic strategy with fewer side effects, especially when combined with agents that can suppress the formation of neutralizing antibodies.

This notice is made in accordance with 35 U.S.C. 209 and 37 CFR Part 404. The prospective Exclusive Patent License will be royalty bearing and may be granted unless within fifteen (15) days from the date of this published notice, the National Cancer Institute receives written evidence and argument that establishes that the grant of the license would not be consistent with the requirements of 35 U.S.C. 209 and 37 CFR Part 404.

Complete applications for a license in the prospective field of use that are timely filed in response to this notice will be treated as objections to the grant of the contemplated Exclusive Patent License. Comments and objections submitted to this notice will not be made available for public inspection and, to the extent permitted by law, will not be released under the *Freedom of Information Act*, 5 U.S.C. 552.

February 21, 2017

Dated

Richard U. Rodriguez
Associate Director
Technology Transfer Center
National Cancer Institute

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